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16. ABSTRACT

The effects of body Pb burden on slow cortical potentials were studied in 63 children aged 13-75 months. Slow wave (SW) voltage during sensory conditioning varied as a linear function of blood lead (PbB) level. The slope of this function, moreover, changed systematically with age. For children under 5 years of age, SW voltage tended to be positive at low PbBs and to be negative above 30 µg/dl. For children over 5 years of age, SW voltage tended to be negative at low PbBs and to be less negative (or positive) above 30 µg/dl. These results provide evidence of altered CNS function at the lowest Pb effect level ever reported.

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EFFECTS OF AGE AND BODY LEAD BURDEN ON CNS FUNCTION IN YOUNG CHILDREN. I. SLOW CORTICAL POTENTIALS

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Considerable evidence indicates that children are at greater risk than adults to nervous system impairment from lead (Pb) exposure (Singhal and Thomas 1980). Lead poisoning produces encephalopathy at blood lead (PbB) levels of 100—120 μg/dl in adults and 80—100 μg/dl in children (Chisholm 1965). Peripheral neuropathies due to chronic occupational exposure have been reported at PbB levels of 50—70 μg/dl in adults (Seppäläinen and Hernberg 1972). Although peripheral Pb neuropathies have rarely been observed in children, subtle behavioral and learning impairments have been associated with PbB levels as low as 40—60 μg/dl (De la Burde and Choate 1972; Perino and Ernhart 1974). The threshold body burden below which no adverse CNS effect occurs, however, is an unresolved question.

One of the difficulties in defining the threshold level for CNS effects of Pb is the relative insensitivity of traditional neurological assessment procedures. Overt symptoms are rarely apparent below 100 μg/dl PbB. Slowed alpha frequency, reduced amplitude, and seizure activity have been observed in the clinical electroencephalogram (EEG) of children with high-level Pb exposures (e.g., Burrows et al. 1951). Low level Pb effects on EEG spectra in children are reported separately (Benignus et al. 1981).

Preliminary evidence (Seppäläinen 1978) suggests that event-related brain potentials (ERPs) provide a sensitive measure of subclinical Pb effects in adults. Seppäläinen observed significant amplitude changes in somatosensory ERPs of battery factory workers with PbBs of 40—70 μg/dl compared to controls. Nerve conduction velocities differed from controls only in workers with PbBs greater than 50 μg/dl. Evoked potential methods have not been used previously to study Pb effects in children.

ERP studies in animal models provide further evidence that Pb exposure produces permanent change in CNS function. Fox et al. (1977, 1979a) have studied the effect of Pb on the visual evoked potential (VEP) in neonatal rats. Fox et al. (1977) found that exposure levels sufficient to yield 65 μg/dl PbB delayed the emergence and increased the latency of primary and secondary VEP components in rat pups. The same rats tested as adults continued to show longer latencies as well as impaired frequency following response compared to controls. VEP amplitude also appears to be permanently altered by neonatal Pb exposure (Fox et al. 1979a).

Selection of appropriate tests to assess the CNS effects of toxicant exposure in young children is a challenging problem. Lelord et al. (1973), John et al. (1977), and others have argued that evoked and slow cortical potentials elicited during sensory conditioning provide useful measures that are free of behavioral and linguistic constraints. In the present study two paradigms were used to elicit slow cortical potentials: (1) an audi-

tory habituation task patterned after Roth (1973), and (2) a classical conditioning paradigm similar to that used by Walter et al. (1964) to elicit contingent negative variation (CNV) in adults. The objectives were to assess the effects of low to moderate body Pb burden on CNS function in young children and to elaborate developmental patterns of slow potentials during sensory conditioning.

Methods

Subjects

One hundred children (53 boys) aged 13–75 months participated in this study. Children were referred by the Wake County Health Department to North Carolina Memorial Hospital (NCMH) on the basis of potential lead exposure through parents employed in lead-related industries or as part of an Early and Periodic Screening, Diagnosis and Treatment Program. Children were asymptomatic at the time of study.

This study was part of a comprehensive neurobehavioral evaluation carried out by the Division for Disorders of Development and Learning at NCMH. Parameters assessed included maternal IQ, child IQ, language development, hyperactivity, and free-field activity level. Pediatric and neurological examinations were administered and extensive demographic data were obtained from parent interviews. Table I summarizes the age, IQ, and socioeconomic status (SES) of children included in the electrophysiological assessment. Most children were from low-income Black families. Questionnaire, interview, and behavioral data have been detailed elsewhere (Milar et al. 1980).

Informed consent for children to participate in the study was obtained from parents prior to testing. Experimental procedures, risks, discomforts, and potential benefits were carefully explained to parents who were paid 25 dollars plus travel expenses to participate in the study.

Data obtained from 11 adults (9 males) aged 18–37 years will be presented for com-

TABLE I

Demographic characteristics and blood lead levels of children *.

Age in months		Blood lead level (μg/dl)							
		7–30			31–59			row means	
		$\bar{X}$	S.D.		$\bar{X}$	S.D.		$\bar{X}$	S.D.
13–25	IQ	94.1	13.8	IQ	87.2	14.9	IQ	91.0	14.5
	SES	68.8	16.9	SES	69.9	10.7	SES	69.3	14.2
	N	16 (9 M, 7 F)		N	13 (8 M, 5 F)		N	29 (17 M, 12 F)	
36–59	IQ	88.1	6.5	IQ	77.9	13.0	IQ	83.4	11.1
	SES	64.0	13.7	SES	68.3	8.1	SES	66.0	11.5
	N	14 (9 M, 5 F)		N	12 (5 M, 7 F)		N	26 (14 M, 12 F)	
60–75	IQ	96.2	14.7	IQ	85.3	10.0	IQ	92.1	13.5
	SES	57.2	7.5	SES	50.7	21.5	SES	54.8	13.3
	N	5 (2 M, 3 F)		N	3 (0 M, 3 F)		N	8 (2 M, 6 F)	
Column means	IQ	92.0	11.6	IQ	83.0	14.0	IQ	88.0	13.4
	SES	65.2	14.8	SES	67.2	12.1	SES	66.1	13.6
	N	35 (20 M, 15 F)		N	28 (15 M, 13 F)		N	63 (33 M, 30 F)	

* Data were broken down in discrete age and PbB groups for tabular presentation only. Regression analyses of continuous distributions were employed for all statistical tests.

parative purposes, but will not be included in statistical analyses. Adult subjects were either parents of children in the study or laboratory personnel.

PbB measurement

Body Pb burden was determined from blood samples obtained from children on the day of evaluation. PbB levels were analyzed by flame atomic absorption spectrometry using the Delves-cup method (Delves 1970). PbBs were not obtained from adults. Investigators were blind to PbB levels of subjects at the time of evaluation.

Data collection

Silver-silver chloride electrodes were used to record EEG from Fpz, Cz, P3 and P4 referred to linked mastoids. The frontal electrode was used to monitor vertical eye movements. EEG was low-pass filtered at 30 Hz (3 dB down). Amplifiers were modified to yield an 8 sec time-constant. Data were digitized on-line at 128 Hz using a PDP-12 computer. Single trial data were plotted for visual editing. Trials with eye movements, blinks, blocking, muscle or other artifacts were eliminated from averages computed off-line.

Testing environment

Testing was done in a small dimly lit double-walled acoustic chamber measuring about 7 m^3 inside. A research assistant was always present and an adult relative was usually present in the chamber. Children under 48 months usually sat in the lap of an adult. Silent 8 mm cartoons were used to engage the attention and minimize eye/body movement artifact. Cartoons were projected on a 50 cm × 77 cm screen located 1.2 m in front of the subject. Cartoons provided an effective means to obtain the cooperation and to limit eye/body movement in children above 30 months of age, although the effectiveness in younger children varied widely. Hand puppets and other props were used to focus the attention and gaze of children who would not watch cartoons. Conversation was discouraged during testing.

Stimulus paradigms

In order to test very young children, two paradigms were employed that required no verbal instruction or motor response. The first consisted of a series of tones (1 kHz, 100 dBA, 30 msec duration, 5 msec rise/fall time) presented through an overhead speaker at 1.5 sec intervals. The standard or 'frequent' tone was replaced by a 'rare' tone (2 kHz) with the same intensity and duration on a pseudorandom schedule every 8—15 presentations. The frequent-rare (FR) paradigm was run for 10—20 min in an attempt to obtain 30 artifact-free trials. Children were asked to sit still and watch cartoons (or hand puppets). Adults were instructed to ignore the tones. Note that the tones were irrelevant to the attended visual modality.

A classical conditioning paradigm which incorporated the attended modality was used for the second test. The 2 kHz tone (conditioned stimulus, CS) as described above was paired with a 1.5 sec blackout (unconditioned stimulus, UCS) of the cartoon. An electromechanical shutter attached to the movie projector was used to produce the blackout period which commenced 1.5 sec after tone onset. The tone occurred pseudorandomly every 12—22.5 sec. The tone-shutter (TS) paradigm followed the FR test without interruption or instruction and was also run for 10—20 min. In order to establish a CS—UCS association, subjects had to attend to the cartoon. The TS paradigm, therefore, could not be used with some of the youngest children (see below). This paradigm was conceived as a passive analog of the fore-period warning task commonly used to elicit the CNV (Walter et al. 1964).

Data analysis

Data from 63 of 100 children were used in the analysis. Subjects were rejected for a variety of reasons including medical, tech-

nical, or behavioral problems. At least 10 artifact-free trials were required for individual subject data from either paradigm to be included in the analysis. Only 13 children under 36 months of age satisfied criteria for inclusion in the TS analysis.

The lack of normative developmental data in the FR paradigm precluded the a priori specification of parameters for statistical testing. Therefore, preliminary exploration of the FR data was undertaken to identify appropriate ERP components for analysis. Components and measurement windows were derived from summary wave forms averaged across age (13—75 months) and PbB levels (7—59 μg/dl) as shown in Fig. 1. A positive component peaking about 160 msec (P160) and a negative component peaking about 500 msec (N500) after the onset of the rare stimulus were selected in this manner. Amplitude and latency measures of the maximal positive peak within a 50—300 msec window and the maximal negative peak within a 150—750 window were computed as in Fig. 1. Mean voltage of a 375 msec prestimulus epoch was used as the baseline for amplitude measures.

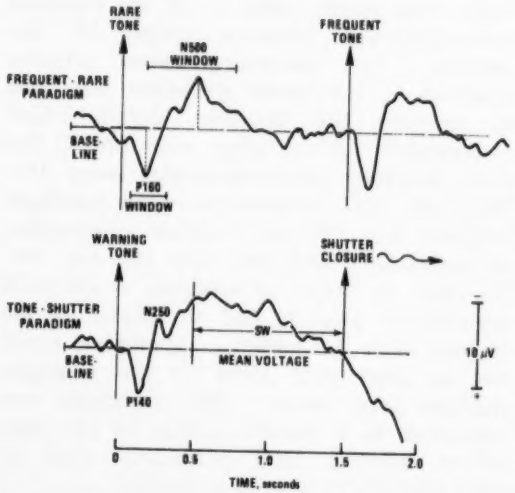

Fig. 1. Measurement parameters. Amplitude and latency of the maximal positive (P160) and negative (N500) peaks following the rare tone were computed from frequent-rare averages. Mean voltage of the slow wave (SW) during a 1 sec epoch preceding shutter closure was computed from tone shutter averages.

Only one a priori measure of TS data was analyzed statistically. Slow wave (SW) amplitude was computed as the mean voltage of a 1 sec interval preceding the blackout period relative to a 350 msec pre-tone baseline (Fig. 1).

Statistical analysis of data from both paradigms was limited to one recording site, the vertex, in order to maximize the power of tests given a fixed α level. A stepwise multivariate procedure employing LINMOD (Christiansen et al. 1979) was used to evaluate results. This procedure entails a weighted least squares linear regression model. This approach might be more accurately termed 'chunkwise' because a *set* of variables, rather than a *single* variable, was tested at each step. Observations were weighted by the square root of the number of trials used in averages. This procedure equalized error variance across subjects and maximized the sensitivity of statistical measures (Draper and Smith 1966). A regression model was chosen as the most efficient test since the distributions of most variables (age, IQ, SES, PbB, and ERPs) were continuous. Any arbitrary grouping of the data would have resulted in a loss of information. The first step was an overall test of the linear effects of demographic variables (age, sex, SES, and IQ). Linear, quadratic, and cubic effects of age and then of PbB were tested in the second and third steps, respectively, using orthogonal polynomials. All 4 linear and quadratic age-by-PbB interactions were tested as a set in the final step. Separate analyses of FR and TS data sets were performed.

In view of the potential implications for human health of the present data set and the lack of developmental norms for the measures chosen, a non-conservative overall α-level of 0.10 was selected. A nominal P value of 0.05 was thus used after Bonferroni correction (Kirk 1968) for separate analyses of FR and TS data.

Results

FR paradigm

Table II shows the results of the multivariate analysis of amplitude and latency measures. None of the measures varied as a function of PbB, PbB × age, IQ, SES or sex. The only significant effect observed in overall tests was age. Stepdown tests indicated that the amplitude and latency of P160, but not N500, varied as linear and cubic functions of age. Estimated amplitude and latency functions derived from the regression model are shown in Fig. 2. The linear trends may be characterized as a general decrease in amplitude and latency with increasing age. The cubic component of the P160 latency-age function accounts for reversals below 22 months and above 60 months. Linear and cubic trends are readily apparent in summary averages constructed for different age groups (Fig. 3) to illustrate developmental changes. Note the apparent polarity inversion of the P160 component and absence of the N500 component in adults.

TS paradigm

Results of the multivariate analysis of the vertex slow wave are shown in Table III. No main effects of demographic variables on SW voltage were observed, but a significant linear interaction between age and PbB was found. That is, SW voltage varied as a linear function of PbB, but the slope of this function changed systematically with age. For children under 5 years of age, SW voltage tended to be positive at low PbB levels, but to be increasingly negative above 30 μg/dl. For children over 5 years of age, SW voltage tended to be negative at low PbB levels and

TABLE II

Results of multivariate regression analysis of frequent-rare paradigm *.

Source	Λ	df (num)	df (den)	$\tilde{F}$	$P <$
Demographics	0.87	12	139.9	0.55	0.88
Age	0.54	12	139.9	2.06	0.0031
lead|age	0.80	12	137.0	0.88	0.58
(Age × PbB)|age	0.62	16	138.1	1.45	0.13
Stepdown tests					
Age on P160 voltage		3	50	3.70	0.0176
Age on P160 latency		3	50	6.91	0.0006
Age on N500 voltage		3	50	0.89	0.46
Age on N500 latency		3	50	0.42	0.75
Age on P160 voltage					
Age linear		1	50	6.53	0.014
Age quadratic		1	50	0.19	0.67
Age cubic		1	50	4.24	0.045
Age on P160 latency					
Age linear		1	50	12.04	0.0011
Age quadratic		1	50	3.86	0.056
Age cubic		1	50	5.69	0.021
Derived regression models					

P1 voltage = $\beta_0 + \beta_1$ (age linear) + β_2 (age cubic), $r^2 = 0.1786$
P1 latency = $\beta_0 + \beta_1$ (age linear) + β_2 (age cubic), $r^2 = 0.2385$

* F approximation for Wilk's likelihood ratio test often yields fractional degrees of freedom.

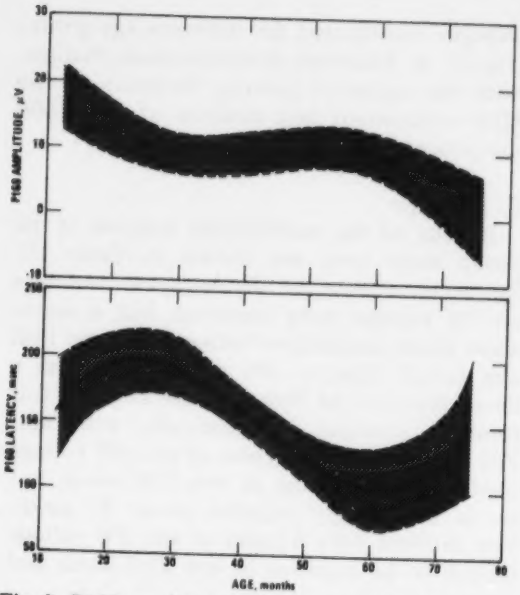

Fig. 2. P160 amplitude and latency plotted as functions of age. Trend lines and 95% confidence bounds were derived from the regression model.

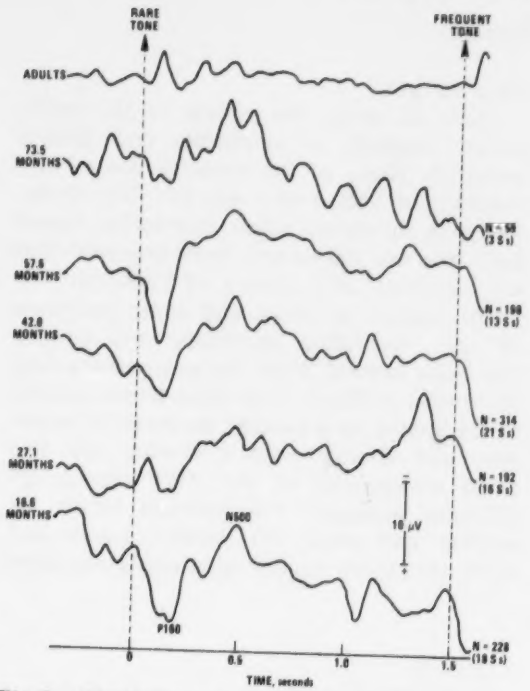

Fig. 3. Developmental pattern of frequent-rare wave form averaged across all artifact-free trials in children of different ages and in adults. Ages shown are the weighted means of children used in each average. Ages were chosen to illustrate prominent features of trends shown in Fig. 2. N = number of trials included in average.

less negative or even positive above 30 μg/dl. The interactive effects of age and PbB on SW voltage are illustrated in Fig. 4.

The linear model derived by stepdown procedures to describe this relationship

TABLE III

Results of multivariate regression analysis of slow wave voltage.

Source	df (num)	df (den)	*F*	*P* <
Demographics	3	37	1.66	0.20
Age	3	37	0.27	0.85
PbB	3	37	2.49	0.08
Age × PbB	4	36	3.08	0.028
Interaction stepdowns				
Age linear × PbB linear	1	36	10.30	0.0028
Age linear × PbB quadratic	1	36	0.16	0.69
Age quadratic × PbB linear	1	36	0.82	0.38
Age quadratic × PbB quadratic	1	36	0.03	0.86
Derived regression models				

SW voltage = $\beta_1 + \beta_1$ (age linear × PbB linear), $r^2 = 0.2225$
SW voltage = $\beta_0 + \beta_1$ (PbB linear) + β_2 (age linear × PbB linear), $r^2 = 0.4407$

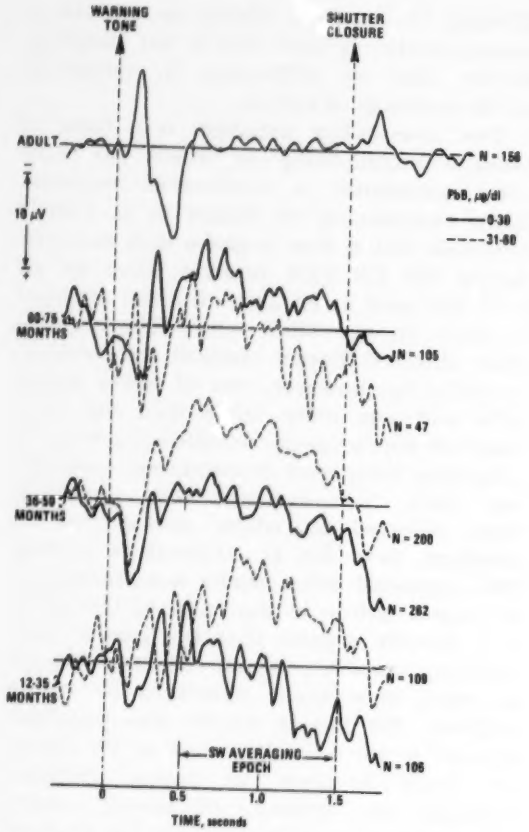

Fig. 4. Interactive effects of age and PbB levels on slow wave voltage during tone-shutter conditioning. Summary averages of all artifact-free trials were constructed for children in three age groups at two different PbB levels. A summary average from adults is included for comparison. Note the absence of any SW in adults. N = number of trials included in average.

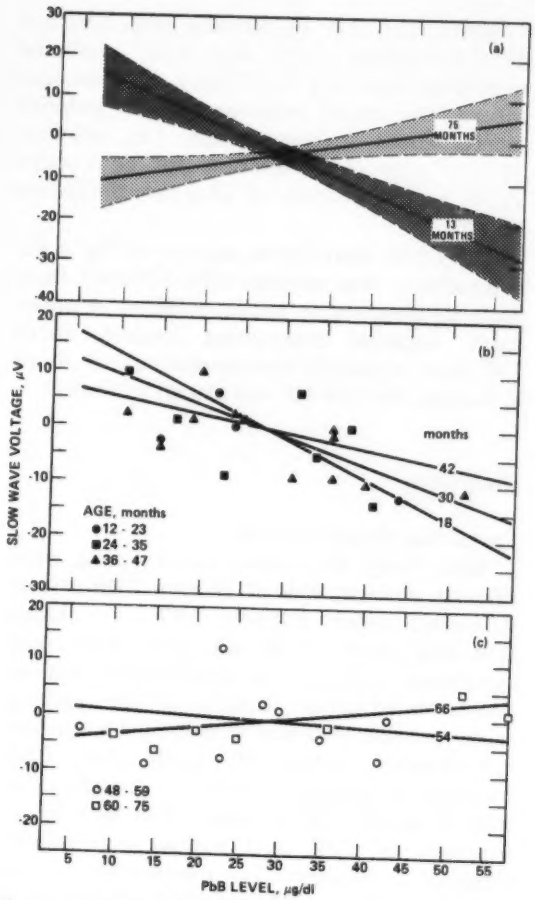

Fig. 5. a: predicted SW voltage and 95% confidence bounds in 13- and 75-month-old children as a function of PbB. b: scatter plots of SW data from children aged 13—47 months with predicted regression lines for ages 18, 30, and 42 months. c: scatter plots for children aged 48—75 months with predicted regression lines for ages 54 and 66 months. These graphs depict the linear interaction of PbB and age.

is:

$$\hat{y} = \hat{\mu} + \hat{\beta}_1 * \text{PbB} + \hat{\beta}_2 * (\text{PbB} \times \text{age})$$

where $\hat{y}$ is the estimated SW voltage, $\hat{\mu}$ is the estimated intercept for the model, $\hat{\beta}_1$ is the estimated regression coefficient for the PbB effect, and $\hat{\beta}_2$ is the estimated regression coefficient for the age-by-PbB interaction. The linear effect of PbB was included in the prediction equation because this component substantially increased the amount of variance accounted for by the model (see Table III). Fig. 5a shows predicted SW voltage and confidence bands as a function of PbB level for the extreme ages represented in the sample. Scatter plots of SW measures for

children aged 13—47 months (Fig. 5b) and 48—75 months (Fig. 5c) with predicted regression lines for 5 arbitrary ages are also shown. The model indicates that SW polarity inverts about 5 years of age, i.e., solution of the regression equation for zero slope yields a predicted age of 58.4 months for no Pb effect.

The adult wave form, shown in Fig. 4 for comparison, was substantially different from patterns observed in young children. A prominent negative component peaked about 140 msec, a positive component peaked about 310 msec, but the SW was absent in adults.

Discussion

Functional considerations

What body Pb burden can a young child tolerate without risk of adverse CNS effect? A recent review (USEPA 1977) concluded that PbB levels of 50—60 μg/dl may cause significant cognitive or sensorimotor impairments in children. Results of the present study provide evidence that body Pb burdens considerably below 30 μg/dl alter CNS function in young children. As illustrated in Figs. 4 and 5, SW voltage varied as a linear function of PbB level within an observed range of 7—59 μg/dl. The relationship of PbB and SW voltage is of particular interest since the data suggest that even very low levels of body Pb burden affect this parameter of brain function, i.e., a 'no effect' threshold does not appear to exist. EEG spectrum measures also indicate effects below 30 μg/dl (Benignus et al. 1981).

These data represent the lowest PbB effect level ever observed in relation to CNS function. The only other biological function known to be affected at such low PbB levels is heme synthesis. Delta-aminolevulinic acid dehydratase activity is inhibited in children and adults at 10 μg/dl (Hernberg et al. 1970). Elevation of erythrocyte protoporphyrin at PbB levels of 15—20 μg/dl has also been reported (Roels et al. 1976). Whether Pb exposure affects the nervous or hematopoietic system first is not presently known due to difficulties in measuring subtle neurological effects.

The tone-shutter paradigm is a form of classical conditioning in which the slow wave constitutes a conditioned response. Early experiments by Walter et al. (1964) indicated that a slow negative shift occurred during the CS—UCS interval when an air puff was used as an unconditioned stimulus to elicit an eye blink reflex. The negative shift obtained during classical (respondent) conditioning, however, was of lower amplitude and was more labile than the CNV observed during operant conditioning wherein a signaled foreperiod reaction-time paradigm was used. No consistent slow potentials were observed in adults during the TS paradigm (see Fig. 4), although a normal CNV appeared when adults were instructed to press a button at the onset of the blackout. Results suggest that the passive conditioning paradigm is an effective vehicle to elicit slow brain potentials in young children, but not in adults. The paradigm appears to be a sensitive test of Pb effects on brain function in young children, although the addition of motor contingencies appears to be necessary for toxicity testing in adults.

The slow wave observed in this study is presumed to be an index of sensory conditioning. The results, therefore, imply that Pb exposure interferes in some way with conditioning or learning in children. This electrophysiological parameter has not been studied in animal models, although impairments in operant conditioning or maze learning have been reported in Pb-exposed dogs, mice, rats and sheep (USEPA 1977). Whether the effects are due to a general learning or specific sensory deficit has not been resolved. Fox et al. (1977) have observed increased latencies in both primary and secondary components of visual evoked potentials (VEPs) of rats exposed neonatally to Pb. Results of Fox et al. suggest that both

sensory and associative levels of CNS function are affected by Pb exposure since primary visual components are considered to reflect activity in specific sensory pathways, while secondary visual components are considered to reflect activity in non-specific pathways associated with attention, perception and learning.

A reversal in the effect of Pb body burden on SW voltage was observed in children as age increased. An interesting parallel occurs in other species. Locomotor activity is the most widely studied behavioral index of lead toxicity in animal models. This extensive literature (reviewed in USEPA 1977) indicates that perinatal lead exposure produces *increased* reactivity of *immature* animals to a novel environment, but *decreased* reactivity in *adult* animals. It should be noted that locomotor activity in young animals appears to be altered only at moderately high exposure levels suggestive of post-encephalopathic sequelae. SW voltage thus appears to be more sensitive than locomotor activity as a measure of Pb effects.

Further evidence of the age-dependent effects of Pb exposure on CNS function has been reported by Fox et al. (1979b). Different patterns of maximal electroshock seizures (MES) were observed in mature and immature rats exposed neonatally to Pb. Immature rats exhibited 'earlier ontogenetic appearance of tonic seizures, increased duration of recovery of righting reflex, and increased seizure severity' compared to controls, i.e., MES responses indicated greater CNS excitability in Pb-exposed than control rats during development. At 60 days of age (adulthood), however, Pb-exposed rats exhibited less excitability to MES than controls as measured by the frequency of hindlimb extension. Differences between Pb-exposed and control groups were enhanced by strychnine, a drug that blocks postsynaptic inhibition in the spinal cord.

Caveats and conclusions

The unique vulnerability of young children to Pb toxicity is well known, although the amount of Pb that can be tolerated without undue risk to human health remains in question. Results of this study suggest that PbB levels well below 30 μg/dl alter CNS function in young children. This effect was apparent in slow cortical potentials as well as EEG spectrum measures (Benignus et al. 1981), two presumably orthogonal measures of CNS function. These findings support a continuum rather than threshold view of Pb toxicity since CNS function appears to be affected across the entire range of exposure (cf., David et al. 1979).

An important caveat should be mentioned in weighing the significance of these findings. The use of blood lead level as an index of body burden is problematic. PbB level is an accurate measure of the amount of Pb circulating in the body at the time of sampling, but an isolated observation reveals little about the exposure history of the individual. A high value could reflect an uncharacteristic, episodic elevation in PbB level, while a low value could belie dangerously high exposures at an earlier (and extremely vulnerable) period of development. If PbB values obtained in the present sample were systematically low across the entire range of observations, a fixed error would be present in the predictor model and CNS effects would be attributed to artificially low body Pb burdens. Alternatively, if random sampling errors were encountered in PbB measures — a more likely possibility — the variance would presumably increase relative to the amount of error. That is, a systematic underestimate of PbB levels would tend to yield a non-conservative error, while random PbB fluctuations would tend to produce a conservative error.

Another caveat concerns the nature of the measures. The paradigms used are experimental, normative data for young children do not exist, and the lack of concurrent behavioral measures limits the assessment of functional significance. Therefore, the present data must be considered preliminary until the results have been repli-

cated. Despite these caveats, this study indicates that slow cortical potentials elicited during sensory conditioning provide a sensitive, non-invasive, non-verbal, and non-motoric tool for studying the neurophysiological sequelae of lead exposure in young children.

Summary

The effects of body Pb burden on slow cortical potentials were studied in 63 children aged 13–75 months. Slow wave (SW) voltage during sensory conditioning varied as a linear function of blood lead (PbB) level. The slope of this function, moreover, changed systematically with age. For children under 5 years of age, SW voltage tended to be positive at low PbBs and to be negative above 30 μg/dl. For children over 5 years of age, SW voltage tended to be negative at low PbBs and to be less negative (or positive) above 30 μg/dl. These results provide evidence of altered CNS function at the lowest Pb effect level ever reported.

Résumé

Effets de l'âge et de la surcharge corporelle en plomb sur le fonctionnement du système nerveux central chez de jeunes enfants. I. Potentiels corticaux lents

Les effets de la charge corporelle en plomb sur les potentiels corticaux lents ont été étudiés chez 63 enfants âgés de 13–75 mois. Le voltage des ondes lentes au cours du conditionnement sensoriel varie comme une fonction linéaire du niveau sanguin de plomb (SPb). La pente de cette fonction, cependant, change systématiquement avec l'âge. Chez des enfants en-dessous de 5 ans, le voltage des ondes lentes tend à être positif pour des SPb bas et à être négatif au-dessus de 30 μg/dl. Pour des enfants âgés de plus de 5 ans, le voltage des ondes lentes tend à être négatif pour des SPb bas et à être moins négatif (ou positif) au-dessus de 30 μg/dl. Ces résultats donnent des preuves d'une altération des fonctions cérébrales pour les niveaux de plomb les plus bas jamais rapportés.

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